Amendments to the Specification:

Please replace the paragraph on page 16, beginning with "Figure 1A," with the following amended paragraph:

Figure [[1A]] 1 (upper profile) shows the mass spectrum of the three peptides (human histidine rich glycoprotein metal-binding domains $(GHHPH)_2G$ (1206 Da), $(GHHPH)_5G$ (2904 Da), and human estrogen receptor dimerization domain (D473-L525) (6168.4 Da)) desorbed in the presence of neutralized energy absorbing molecules (sinapinic acid, pH 6.2). Figure [[1B]] 1 (lower profile) shows the sequential in situ metal (Cu)-binding of the peptides in the presence of neutral energy absorbing molecules.

Please replace the paragraph bridging pages 16 and 17, beginning with "Figure 2A," with the following amended paragraph:

Figure [[2A]] 2 (top profile) shows the mass spectrum of the human casein phosphopeptide (5P, 2488 Da) desorbed in the presence of neutralized energy absorbing molecules (sinapinic acid, pH 6.5). Figure [[2B]] 2 (second from top profile) shows the sequential in situ 5 min alkaline phosphatase digestion to remove phosphate groups from the phosphopeptide. Figure [[2C]] 2 (third from top profile) shows the mass spectrum of the phosphopeptide after further in phosphatase digestion in the presence of acidic energy absorbing molecules (2,5 dihydroxybenzoic acid, pH 2) as described in prior art.

Please replace the paragraph on page 17, beginning with "Figure 5," with the following amended paragraph:

Figure [5, profile A] 5A, top profile, shows the mass spectrum of sperm activating factor (933 Da) and neurotensin (1655 Da) (and their multiple Na-adducts) in the peptide solution unadsorbed by the IDA-Cu(II) surface. Figure [5, profile B] 5A, middle profile, shows the mass spectrum of angiotensin I (1296.5 Da) plus Na-adduct peaks that were selectively

adsorbed on the IDA-Cu(II) surface. Figure [5, profile C] 5A, bottom profile, and Figure [6, profile C] 5B, bottom profile, show the mass spectrum of the same angiotensin I adsorbed on IDA-Cu(II) after water wash. Figure [6, profile D] 5B, middle profile, shows the sequential in situ copper-binding (1 and 2 Cu) by affinity adsorbed angiotensin I. Figure [6, profile E] 5B, top profile, shows the sequential in situ trypsin digestion of the affinity adsorbed angiotensin I.

Please replace the paragraph on page 18, beginning with "Figure 7," with the following amended paragraph:

Figure [[7]] 6 shows the mass spectrum of myoglobin (4 to 8 fmole) affinity adsorbed on IDA-Cu(II) surface.

Please replace the paragraph on page 18, beginning with "Figure 8," with the following amended paragraph:

Figure [[8]] 7 (top profile) shows the mass spectrum of synthetic casein peptide (1934 Da) with multiple phosphorylated forms affinity adsorbed from a crude mixture on TED-Fe(III) surface. After sequential in situ alkaline phosphatase digestion, only the original nonphosphorylated form remained (lower profile).

Please replace the paragraph on page 18, beginning with "Figure 9," with the following amended paragraph:

Figure [9, profile A] 8, bottom profile, shows the mass spectrum of total proteins in infant formula. Figure [9, profile B] 8, second from bottom profile, shows the mass spectrum of phosphopeptides in infant formula affinity adsorbed on TED-Fe(III) surface. Figure [9, profile C] 8, second from top profile, shows the mass spectrum of total proteins in gastric aspirate of preterm infant obtained after feeding the infant formula. Figure [9, profile D] 8, top

profile, shows the mass spectrum of phosphopeptides in the gastric aspirate affinity adsorbed on TED-Fe(III) surface.

Please replace the paragraph bridging pages 18 and 19, beginning with "Figure 10A," with the following amended paragraph:

Figure [[10A]] 9A shows the composite mass spectra of human and bovine histidine-rich glycoprotein adsorbed on IDA-Cu(II) surface before and after N-glycanase digestion. The mass shifts represent the removal of carbohydrate from the respective glycoproteins. Figure [[10B]] 9B shows the composite mass spectra of trypsin digested peptides from the deglycosylated proteins of the two species (top profile for human protein, second from bottom profile for bovine protein) and in situ Cu(II)-binding of the trypsin digested peptides of the two species (second from top profile for human protein, bottom profile for bovine protein; the numbers 1, 2 indicate the number of copper bound). Figure [[10C]] 9C shows that one such Cu(II)-binding peptide (bottom profile) has at least 4 His residues which are specifically modified by diethylpyrocarbonate to form 4 N-carbethoxy-histidyl adducts (1-4, top profile). Figure [[10D]] 9D shows the partial C-terminal sequence of the major Cu-binding peptide in the bovine histidine rich glycoprotein.

Please replace the paragraph on page 19, beginning with "Figure 11," with the following amended paragraph:

Figure [[11]] 10 (bottom profile) shows the mass spectrum of rabbit anti-human lactoferrin immunoglobulin alone (control) affinity adsorbed on sheep anti-rabbit IgG paramagnetic surface. The top profile shows the mass spectrum of human lactoferrin and rabbit anti-human lactoferrin immunoglobulin complex affinity adsorbed on sheep anti-rabbit IgG paramagnetic surface.

Please replace the paragraph on page 19, beginning with "Figure 12," with the following amended paragraph:

Figure [[12]] 11A shows the mass spectrum of human lactoferrin affinity adsorbed from preterm infant urine on a anti-human lactoferrin immunoglobulin nylon surface. Figure [[13]] 11B shows the equivalent mass spectrum of whole preterm infant urine containing 1 nmole/ml of lactoferrin.

Please replace the paragraph on page 19, beginning with "Figure 14," with the following amended paragraph:

Figure [[14]] 12 (lower profile) shows the mass spectrum of pure bovine histidine rich glycoprotein. The upper profile shows the mass spectrum of bovine histidine rich glycoprotein and fragments affinity adsorbed from bovine colostrum on anti-bovine histidine rich glycoprotein immunoglobulin surface.

Please replace the paragraph on page 20, beginning with "Figure 15," with the following amended paragraph:

Figure [[15]] 13 shows the composite mass spectra of the peptides of follicle stimulating hormone recognized by the different anti-follicle stimulating hormone antibodies.

Please replace the paragraph on page 20, beginning with "Figure 16," with the following amended paragraph:

Figure [[16]] 14 shows the mass spectrum of human lactoferrin affinity adsorbed on a single bead of single-stranded DNA agarose deposited on a 0.5 mm diameter probe element.

Please replace the paragraph on page 20, beginning with "Figure 17," with the following amended paragraph:

Figure [[17]] 15 shows the mass spectrum of human lactoferrin affinity adsorbed from preterm infant urine on single-stranded DNA surface.

Please replace the paragraph on page 20, beginning with "Figure 18A," with the following amended paragraph:

Figure[[18A]] 16A shows the composite mass spectra of the total proteins in human duodenal aspirate (lower profile) and the trypsin affinity adsorbed from the aspirate on a soybean trypsin inhibitor surface (upper profile). Figure [[18B]] 16B stows the mass spectrum of trypsin affinity adsorbed from 1 ul of aspirate on a soybean trypsin inhibitor nylon surface.

Please replace the paragraph on page 20, beginning with "Figure 19A," with the following amended paragraph:

Figure [[19A]] 17A shows the mass spectrum of biotinylated insulin affinity adsorbed from human urine on a Streptavidin surface. Figure [[19B]] 17B shows the mass spectrum of biotinylated insulin affinity adsorbed from human plasma on a Streptavidin surface.

Please replace the paragraph bridging pages 20 and 21, beginning with "Figure 20," with the following amended paragraph:

Figure [[20]] 18 (upper profile) shows the mass spectrum of total proteins in human serum. Figure [[20]] 18 (lower profile) shows the mass spectrum of serum albumin affinity adsorbed from human serum on a Cibacron-blue surface.

Please replace the paragraph on page 21, beginning with "Figure 21," with the following amended paragraph:

Figure [[21]] 19 shows the molecular structure of surface bound cinnamamide; R represents the surface plus cross-linker.

Please replace the paragraph on page 21, beginning with "Figure 22," with the following amended paragraph:

Figure [[22]] 20 (upper profile) shows the mass spectrum of peptide mixtures desorbed from surface bound cinnamamide. Figure [[20B]] 20 (lower profile) shows the mass spectrum of the same peptide mixtures with free cinnamamide.

Please replace the paragraph on page 21, beginning with "Figure 23," with the following amended paragraph:

Figure [[23]] 21 shows the molecular structure of surface bound cinnamyl bromide; R represents the surface plus cross-linker.

Please replace the paragraph on page 21, beginning with "Figure 24," with the following amended paragraph:

Figure [[24]] 22 (upper profile) shows the mass spectrum of peptide mixtures desorbed from surface bound cinnamyl bromide. Figure [[22B]] 22 (lower profile) shows the mass spectrum of the same peptide mixtures with free cinnamyl bromide.

Please replace the paragraph on page 21, beginning with "Figure 25," with the following amended paragraph:

Figure [[25]] 23 shows the molecular structure of surface bound MAP-dihydroxybenzoic acid; R represents the surface plus cross-linker.

Please replace the paragraph bridging pages 21 and 22, beginning with "Figure 26," with the following amended paragraph:

Figure [[26]] 24 (upper profile) shows the mass spectrum of peptide mixtures desorbed from surface bound MAP alone. Figure [[26]] 24 (lower profile) shows the mass spectrum of the same peptide mixtures desorbed from surface bound MAP-dihydroxybenzoic acid.

Please replace the paragraph on page 22, beginning with "Figure 27A," with the following amended paragraph:

Figure [[27A]] 25A shows the mass spectrum (1,200-50,000 m/z region) of myoglobin desorbed from surface bound α-cyano-4-hydroxycinnamic acid. Figure 25B shows the same mass spectrum in the low mass region (0-1200 m/z).

Please replace the paragraph on page 22, beginning with "Figure 28," with the following amended paragraph:

Figure [[28]] 26 shows the molecular structure of energy absorbing molecules bound to polyacrylamide or nylon or acrylic surface via glutaraldehyde activation.

Please replace the paragraph on page 22, beginning with "Figure 29," with the following amended paragraph:

Figure [[29]] 27 shows the molecular structure of energy absorbing molecules bound to polyacrylamide or nylon or acrylic surface via divinyl sulfone activation.

Please replace the paragraph on page 22, beginning with "Figure 30," with the following amended paragraph:

Figure [[30]] 28 shows the molecular structure of energy absorbing molecules bound to polyacrylamide or nylon or acrylic surface via dicyclohexylcarbodiimide activation.

Please replace the paragraph on page 22, beginning with "Figure 31," with the following amended paragraph:

Figure [[31]] 29 shows the molecular structure of energy absorbing molecules bound to polyacrylamide or nylon or acrylic surface with multiple antigenic peptide via dicyclohexylcarbodiimide activation.

Please replace the paragraph on page 23, beginning with "Figure 32," with the following amended paragraph:

Figure [[32]] 30 shows the molecular structure of thiosalicylic acid bound to iminodiacetate (IDA)-Cu(II) surface.

Please replace the paragraph on page 23, beginning with "Figure 33," with the following amended paragraph:

Figure [[33]] 31 shows the mass spectrum of human estrogen receptor dimerization domain desorbed from thiosalicylic acid-IDA-Cu(II) surface.

Please replace the paragraph on page 23, beginning with "Figure 34," with the following amended paragraph:

Figure [[34]] 32 shows the molecular structure of α-cyano-4-hydroxycinnamic acid bound to DEAE surface.

Please replace the paragraph on page 23, beginning with "Figure 35," with the following amended paragraph:

Figure [[35]] 33A shows the mass spectrum of human estrogen receptor dimerization domain desorbed from sinapinic acid-DEAE surface. Figure 33B shows the mass spectrum of myoglobin desorbed from α-cyano-4-hydroxycinnamic acid DEAE surface.

Please replace the paragraph on page 23, beginning with "Figure 36," with the following amended paragraph:

Figure [[36]] 34 shows the molecular structure of α-cyano-4hydroxycinnamic acid bound to polystyrene surface.

Please replace the paragraph on page 23, beginning with "Figure 37," with the following amended paragraph:

Figure [[37]] 35 shows the C-terminal sequence analysis of surface immobilized via photolytic bond histidine rich glycoprotein metal binding domain.

Please replace the paragraph on page 42, beginning with "In a preferred embodiment," with the following amended paragraph:

In a preferred embodiment, the analyte is selectively desorbed from the mixture after impingement by the energy source. In another preferred embodiment, the affinity devices are arranged in predetermined arrays. This can be accomplished by arranging the affinity adsorption "spots" (0.005 to 0.080 inch diameter) on the probe surface in a defined manner (400 to 1,000 spots could be placed on a surface about the size of a glass slide). In a more preferred embodiment, the arrays selectively absorb a plurality of different analytes.

Please replace the paragraph bridging pages 47 and 48, beginning with "1. Sinapinic acid (Aldrich Chemical Co.," with the following amended paragraph:

1. Sinapinic acid (Aldrich Chemical Co., Inc., Milwaukee, Wis.) is suspended in water at 20 mg/ml (pH 3.88) and neutralized with triethylamine (Pierce, Rockford, Ill.) to pH 6.2-6.5. An aqueous mixture (1 μl) of synthetic peptides, containing human histidine rich glycoprotein metal-binding domains $(GHHPH)_2G$ (1206 Da), $(GHHPH)_5G$ (2904 Da), and human estrogen receptor dimerization domain (D473-L525) (6168.4 Da) is mixed with 2 μl sinapinic acid (20 mg/ml water, pH 6.2) on a probe tip and analyzed by laser desorption time-of-flight mass spectrometry. After acquiring five spectra (average 100 laser shots per spectrum), the probe is retrieved, 2 μl of 20 mM $Cu(SO)_4$ is added and the sample is reanalyzed by mass spectrometry. Figure [[1A]] 1 (upper profile) shows the mass spectrum of the three peptides desorbed in the presence of neutralized energy absorbing molecules. Figure [[1B]] 1 (lower profile) shows the in situ metal-

situ metal-binding of the peptides in the presence of neutral energy absorbing molecules. The $(GHHPH)_2G$ peptide can bind at least 4 Cu(II), the $(GHHPH)_5G$ peptide can bind at least 5 Cu(II) and the dimerization domain can bind at least 1 Cu(II) under the present experimental conditions. Similar result is obtained with α-cyano-4-hydroxycinnamic acid (20 mg/ml water) neutralized to pH 6.5.

Please replace the paragraph bridging pages 48 and 49, beginning with "2. An aliquot of," with the following amended paragraph:

2. An aliquot of 1 μl of human β casein phosphopeptide (R1-K18+5P) (2488 Da) is mixed with 1 μl of sinapinic acid (20 mg/ml water) neutralized to pH 6.5, and analyzed by laser desorption time-of-flight mass spectrometry. After acquiring five spectra (average 100 laser shots per spectrum), the probe is removed, the remaining phosphopeptide mixed with the neutralized sinapinic acid is digested directly on the probe tip by 0.5 μl of alkaline phosphatase (Sigma) and incubated at 23°C for 5 min. After acquiring five spectra (average 100 laser shots per spectrum), the probe is removed, further digestion on remaining phosphopeptides is carried out by adding another aliquot of 0.5 μl of alkaline phosphatase and incubated at 23°C for 5 min. The sample is re-analyzed by laser desorption mass spectrometry. Figure [[2A]] 2 (top profile) shows the mass spectrum of the phosphopeptide desorbed in the presence of neutralized energy absorbing molecules. Figure [[2B]] 2 (second from top profile) shows the in situ 5 min alkaline phosphatase digestion to remove phosphate groups from the phosphopeptide. The 0P, 1P and 3P peaks represent the products after removal of five, four and two phosphate groups respectively from the phosphopeptide. Figure [[2C]] 2 (third from top profile) shows that further in situ digestion with alkaline phosphatase can result in almost complete removal of all phosphate groups from the phosphopeptide. In contrast, Figure [[2D]] 2 (bottom profile) shows that in the control experiment where in situ alkaline phosphatase (0.5 μl) digestion is carried out in the presence of energy absorbing molecules without prior neutralization (e.g., sinapinic acid at pH 3.88 or dihydroxybenzoic acid at pH 2.07), very limited digestion occurred in 10 min at 23°C.

Please replace the paragraph bridging pages 52 and 53, beginning with "1. Cu(II) ion is chelated by iminodiacetate" with the following amended paragraph:

1. Cu(II) ion is chelated by iminodiacetate (IDA) group covalently attached to either porous agarose beads (Chelating Sepharose Fast Flow, Pharmacia Biotech Inc., Piscataway, N.J., ligand density 22-30 μmole/ml gel) or solid silica gel beads (Chelating TSK-SW, ToyoSoda, Japan, ligand density 15-20 .mu.mole/ml gel). A mixture of synthetic peptides containing neurotensin (1655 Da), sperm activating peptide (933 Da) and angiotensin I (1296.5 Da), is mixed with 50 μl packed volume of TSK-SW IDA-Cu(II) at pH 7.0 (20 mM sodium phosphate, 0.5M sodium chloride) at 23°C for 10 min. The gel is separated from the remaining peptide solution by centrifugation and is then washed with 200 μl sodium phosphate, sodium chloride buffer, pH 7.0 three times to remove nonspecifically bound peptides. Finally, the gel is suspended in 50 μl of water. Aliquots of 2 μl gel suspension and nonadsorbed peptide solution are mixed with 1 μl of sinapinic acid (dissolved in methanol) on a stainless steel probe tip and analyzed by laser desorption time-of-flight mass spectrometry. After acquiring five spectra (average of 100 laser shots per spectrum) on various spots of the probe tip, the sinapinic acid is removed by methanol. An aliquot of 2 μl of 20 mM $CuSO_4$ is added, then mixed with 1 μl of sinapinic acid and reanalyzed by laser desorption time-of-flight mass spectrometry. After acquiring another five spectra (average of 100 laser shots per spectrum) on various spots of the probe tip, the sinapinic acid is removed by methanol. The remaining peptide adsorbed on IDA-Cu(II) gel beads is then digested with 1 μl of trypsin (Sigma) in 0.1M sodium bicarbonate, pH 8.0 at 23°C for 10 min in a moist chamber. The gel beads are then washed with water to remove enzyme and salt before 1 μl of sinapinic acid is added and the sample analyzed by laser desorption time-of-flight mass spectrometry. Figure 5A, top profile, shows the molecular ions (and multiple Na-adducts) of sperm activating factor (933 Da) and neurotensin (1655 Da) in the remaining peptide solution unabsorbed by the IDA-Cu(II). There is no significant peak corresponding to angiotensin I (1296.5 Da). The mass spectrum in Figure [[5B]] 5A, middle profile, shows the angiotensin I

plus Na-adduct peaks that are selectively adsorbed on the IDA-Cu(II) gel. When the IDA-Cu(II) gel is further washed with 500 .mu.l of water two times, the resulting mass spectrum shows only the parent angiotensin I ion and no other adduct peaks (Figures [[5]] 5A and ~~6, profiles C~~ 5B, bottom profiles). Figure [[6D]] 5B, middle profile, shows the *in situ* copper binding (1 and 2 Cu) by the angiotensin peptide. Figure [[6E]] 5B, top profile, shows the *in situ* trypsin digestion of the angiotensin peptide at the single Arg2 position in the sequence.

Please replace the paragraph bridging pages 54 and 55, beginning with "2. A solution of horse heat myoglobin" with the following amended paragraph:

2. A solution of horse heart myoglobin (325 pmole, 16,952 Da) is mixed with 50 µl of TSK-SW IDA-Cu(II) at pH 7.0 (20 mM sodium phosphate, 0.5M sodium chloride) at 23°C for 10 min. The gel is separated from the solution by centrifugation and then washed with 500 µl of buffer two times and 500 µl of water two times. The quantity of remaining myoglobin in all these solutions are then estimated spectrophotometrically, the quantity adsorbed on the gel can then be calculated. The gel is suspended in 50 µl of water and then serially diluted into water. An aliquot of 0.5 µl of the diluted gel suspension is mixed with 1 µl of sinapinic acid (dissolved in 30% methanol, 0.1% trifluoroacetic acid) and analyzed by laser desorption time-of-flight mass spectrometry. Figure [[7]] 6 shows that a detectable signal (signal/noise=6, after averaging 50 laser shots) of myoglobin is obtained with a calculated quantity of 4 to 8 fmole deposited on the probe tip.

Please replace the paragraph bridging pages 55 and 56, beginning with "3. The human ß casein peptides" with the following amended paragraph:

3. The human ß casein peptides (E2-K18) are synthesized on an Applied Biosystem Model 430A Peptide Synthesizer using the NMP-HOBt protocol. The Ser residues to be phosphorylated are coupled to the peptide chain without side chain protecting group. The

unprotected Ser are first phosphinylated using di-t-butyl-N,N,-diisopropyl-phosphoramidite. The phosphite ester is then oxidized with t-butyl peroxide, washed, and cleaved from the resin. All the side chain protecting groups are removed with 95% trifluoroacetic acid. The crude phosphopeptides are extracted with methyl tbutyl ether and dried. This crude preparation of synthetic phosphopeptides is dissolved in 50 mM MES, 0.15M sodium chloride, pH 6.5 and mixed with 50 µl of tris(carboxymethyl)-ethylenediamine (TED)-Fe(III) immobilized on porous Sepharose (synthesized as described by Yip, T.-T. and Hutchens, T. W., Protein Expression and Purification 2: 355-362 (1991), ligand density 65 µmole/ml) at 23°C for 15 min. The gel is washed with 500 µl of the same buffer three times and then with 500 µl of water once. An aliquot of 1 µl of gel is mixed with 1 µ l of sinapinic acid (dissolved in 30% methanol, 0.1% trifluoroacetic acid) on the probe tip and analyzed by laser desorption time-of-flight mass spectrometry. After acquiring five spectra (average of 100 laser shots per spectrum) on various spots of the probe tip, the sinapinic acid is removed by methanol, and the remaining phosphopeptides adsorbed on TED-Fe(III) is digested directly on the probe tip by 1 µl of alkaline phosphatase (ammonium sulfate suspension, Sigma) in 50 mM HEPES pH 7.0 at 23°C for 10 min. in a moist chamber. The gel is washed with water to remove enzyme and salt. Sinapinic acid is added and the sample is reanalyzed by laser desorption time-of-flight mass spectrometry. Figure [[8]] 7 (top profile) shows the distribution of casein peptide (1934 Da) with multiple phosphorylated forms. After in situ alkaline phosphatase digestion, only the original nonphosphorylated form remains (lower profile).

Please replace the paragraph bridging pages 56 and 57, beginning with "4. Aliquots of 100 µl of preterm infant formula" with the following amended paragraph:

4. Aliquots of 100 µl of preterm infant formula (SIMILAC, Meade Johnson) and gastric content of preterm infant aspirated 90 min after feeding of the formula are mixed with 50 µl of TED-Fe(III) Sepharose in 0.1M MES, 0.15M sodium chloride, pH 6.5 at 23°C for 15 min. The gel is washed with 500 µl of the same buffer three times and then with 500 µl of water once. Aliquots of 1 µl of gel suspensions or preterm infant formula or gastric aspirate are mixed with 2 µl of

sinapinic acid (dissolved in 50% acetonitrile, 0.1% trifluoroacetic acid) on the probe tip and analyzed by laser desorption time-of-flight mass spectrometry. Figure [[9]] 8 shows that the mass spectrum of whole gastric aspirate (second from top profile) is quite similar to that of whole infant formula (bottom profile) in the 1,000-15,000 Da region. However, the mass spectra of analytes selectively adsorbed by TED-Fe(III) from the two samples are quite different, there are more low molecular weight phosphopeptides (*i.e.,* bound by TED-Fe(III)) present in the gastric aspirate (top profile) than in the formula (second from bottom profile) due to the gastric proteolytic digestion of phosphoproteins present in the formula.

Please replace the paragraph bridging pages 57-59, beginning with "5. Aliquots of 200 µl of human and bovine" with the following amended paragraph:

5. Aliquots of 200 µl of human and bovine histidine-rich glycoprotein are mixed with 50 µl of IDA-Cu(II) Sepharose (Pharmacia) at pH 7.0 (20 mM sodium phosphate, 0.5M sodium chloride) at 23°C for 10 min. The gel is washed with 500 µl buffer two times and 500 µl water once. Aliquots of 1 µl of gel are mixed with 2 µl of sinapinic acid (dissolved in 30% methanol 0.1% trifluoroacetic acid) and analyzed by laser desorption time-of-flight mass spectrometry. After acquiring five spectra (average of 100 laser shots per spectrum) on various spots of the probe tip, the sinapinic acid is removed by methanol wash. The remaining glycoproteins adsorbed on the IDA-Cu(II) gel is then digested with N-glycanase in 20 mM sodium phosphate, 0.5M sodium chloride, 3M urea, pH 7.0 at 37°C overnight in a moist chamber. After washing with water to remove enzyme and salt, 2 µl of sinapinic acid is added and the sample is analyzed by mass spectrometry. After acquiring five spectra (average of 100 laser shots per spectrum) on various spots of the probe tip, the sinapinic acid is removed by methanol. Aliquots of 2 µl of trypsin in 0.1M sodium bicarbonate are added and incubated at 37°C for 30 min in a moist chamber. After a water wash to remove enzyme and salt, sinapinic acid is added and the sample is analyzed by mass spectrometry. After acquiring five spectra (average of 100 laser shots per spectrum) on various spots of the probe tip, the sinapinic acid is removed by methanol. Aliquots of 2 µl of

20 mM $CuSO_4$ is added. This is followed by addition of 2 µl of sinapinic acid and then analyses by mass spectrometry. After acquiring five spectra (average of 100 laser shots per spectrum) on various spots of the probe tip, the sinapinic acid is removed by methanol. Aliquots of 2 µl of diethylpyrocarbonate (Sigma) in 5 mM HEPES, pH 6.5 are added and incubated at 23°C for 30 min. After a water wash to remove chemicals and buffer salts, 2 µl of sinapinic acid is added and the sample is analyzed by mass spectrometry. To obtain a partial sequence of the metal-binding peptides, instead of modifying the histidine residues with diethylpyrocarbonate, add 1 µl of carboxypeptidase Y (Boehringer Mannheim) to the tryptic digest adsorbed on the surface and incubate at room temperature in a moist chamber for 5 min. Wash away the enzyme and salt with water, add 1 µl of sinapinic acid and analyze by mass spectrometry. Figure [[10A]] 9A shows the composite mass spectra of human and bovine histidine-rich glycoprotein adsorbed on IDA-Cu(II) Sepharose before and after N-glycanase digestion. The mass shifts represent the removal of carbohydrate from the respective glycoproteins. Figure [[10B]] 9B shows the composite mass spectra of trypsin digested peptides from the deglycosylated proteins of the two species (top profile for human protein, second from bottom profile for bovine protein) and *in situ* Cu(II)-binding of the trypsin digested peptides of the two species (second from top profile for human protein, bottom profile for bovine protein; the numbers 1, 2 indicate the number of copper bound). Figure [[10C]] 9C shows that one such Cu(II)-binding peptide (bottom profile) has at least 4 His residues which are specifically modified by diethylpyrocarbonate to form 4 N-carbethoxy-histidyl adducts (1-4, top profile). Figure [[10D]] 9D shows the partial C-terminal sequence of the major Cu-binding peptide in the bovine histidine rich glycoprotein. This example illustrates the effective use of SEAC to probe the structure and function of metal-binding domains of proteins from different species.

Please replace the paragraph bridging pages 59 and 60, beginning with "1. Polyclonal rabbit anti-human lactoferrin" with the following amended paragraph:

1. Polyclonal rabbit anti-human lactoferrin antibody is custom generated against purified human lactoferrin by Bethyl Laboratories (Montgomery, Tex.). The antibody is affinity-purified by thiophilic adsorption and immobilized lactoferrin columns. Sheep anti-rabbit IgG covalently attached to magnetic beads are obtained from Dynal AS, Oslo, Norway (uniform 2.8 μm supermagnetic polystyrene beads, ligand density 10 μg sheep IgG per mg bead). Human lactoferrin (1 nmole, ^{59}Fe-labeled, 81,100 Da) is incubated with rabbit anti-human lactoferrin antibody in 20 mM sodium phosphate, 0.15M sodium chloride, pH 7.0 at 37°C for 30 min. Subsequently, 40 μl of sheep anti-rabbit IgG on Dynabeads (6-7 x 10^8 beads/ml) is added and incubated at 37°C for 30 min. The beads are washed with 500 μl of sodium phosphate buffer three times and 500 μl water two times. The final amount of human lactoferrin bound to the complex is estimated to be 4 pmole. Approximately one-tenth of the beads is transferred to a teflon-coated magnetic probe tip, mixed with 2 μl of sinapinic acid (dissolved in 30% methanol, 0.1% trifluoroacetic acid) and analyzed by laser desorption time-of-flight mass spectrometry. Figure [[11]] 10 shows the presence of lactoferrin (81,143 Da) in the antigen-primary antibody-secondary antibody complex (upper profile), whereas the primary antibody-secondary antibody control (lower profile) shows only the rabbit antibody signal (149,000 Da for singly charged, and 74,500 Da for the doubly charged).

Please replace the paragraph on page 61, beginning with "2. Affinity-purified rabbit anti-human" with the following amended paragraph:

2. Affinity-purified rabbit anti-human lactoferrin is covalently bound to the tip of an activated nylon probe element (2 mm diameter) via glutaraldehyde. This is immersed in 1 ml of preterm infant urine, pH 7.0, containing 350 fmole of human lactoferrin and stirred at 4-8°C for 15 hr. The nylon probe tip is removed and washed with 1 ml of 20 mM sodium phosphate, 0.5M sodium chloride, 3M urea, pH 7.0 three times and 1 ml of water two times. An aliquot of 2 μl of sinapinic acid (dissolved in 30% methanol, 0.1% trifluoroacetic acid) is added and the sample is analyzed by laser desorption time-of-flight mass spectrometry. Figure [[12]] 11A shows the

human lactoferrin molecular ion (signal/noise=2.5, average of 25 laser shots) in the mass spectrum. Figure [[13]] 11B shows the equivalent mass spectrum of whole preterm infant urine containing 1 nmole/ml of lactoferrin; the signal suppression caused by the presence of other components in the urine sample is so severe that even addition of several thousand fold excess over 350 fmole/ml of lactoferrin as described for Figure [[12]] 11A can not be detected.

Please replace the paragraph on page 63, beginning with "5. Polyclonal rabbit anti-bovine histidine rich" with the following amended paragraph:

5. Polyclonal rabbit anti-bovine histidine rich glycoprotein antibody is custom generated against purified bovine histidine rich glycoprotein by Bethyl Laboratories (Montgomery, Tex.). The antibody is affinity-purified by thiophilic adsorption and immobilized bovine histidine rich glycoprotein columns. The purified antibody is immobilized on AffiGel 10 (BioRad Laboratories, Hercules, Calif., ligand density 15 μmole/ml gel) according to manufacturer's instruction. An aliquot of 200 μl of bovine colostrum is diluted with 200 μl of 20 mM sodium phosphate, pH 7.0 and mixed with 50 μl of immobilized antibody at 23°C for 30 min. The gel is washed with 500 μl of 20 mM sodium phosphate, 0.5M sodium chloride, 3M urea, pH 7.0 three times and 500 μl of water two times. An aliquot of 1 μl of the washed gel is mixed with 2 μl of sinapinic acid (dissolved in 30% methanol, 0.1% trifluoroacetic acid) on the probe tip and analyzed by laser desorption time-of-flight mass spectrometry. Figure [[14]] 12 shows the composite mass spectra of purified bovine histidine rich glycoprotein (lower profile) and proteins affinity adsorbed from bovine colostrum (upper profile). The result indicates the presence of intact histidine rich glycoprotein and its major proteolytic fragments in bovine colostrum.

Please replace the paragraph bridging pages 64 and 65, beginning with "6. Antibody epitope mapping is easily achieved" with the following amended paragraph:

6. Antibody epitope mapping is easily achieved with the SEAC technique. Three different sources of anti-human follicle stimulating hormone (a polyclonal specific against beta FSH from Chemicon International, Temecula, Calif., a monoclonal specific against beta 3 epitope from Serotec, Indianapolis, Ind., a monoclonal from Biodesign, Kennebunk, Me.) are immobilized on AffiGel 10 according to manufacturer's instruction. These immobilized antibodies are all tested to bind specifically the follicle stimulating hormone by incubating with two different preparations of follicle stimulating hormone (a semipure preparation from Chemicon, and a crude preparation from Accurate Chemical and Scientific Corp.) and then analyzed by mass spectrometry in the presence of sinapinic acid. Then the semipure preparation of human FSH (Chemicon) is digested with trypsin and separate aliquots (7 ul) are reacted with the immobilized antibodies (10 ul of 1:1 gel suspension) in phosphate-buffered saline at 4°C for 2 hr. After washing with phosphate-buffered saline and water, the adsorbed proteins are analyzed by laser desorption mass spectrometry in the presence of sinapinic acid. Figure [[15]] 13 shows the composite mass spectra of the peptides of follicle stimulating hormone recognized by the different antibodies. The two monoclonal antibodies clearly recognize different epitopes, whereas the polyclonal recognizes multiple epitopes common to those recognized by both monoclonals.

Please replace the paragraph on page 65, beginning with "1. Single-stranded DNA immobilized on 4% agarose" with the following amended paragraph:

1. Single-stranded DNA immobilized on 4% agarose beads are obtained from GIBCO BRL (Gaithersburg, Md., ligand density 05-1.0 mg DNA/ml gel). An aliquot of ^{125}I-human lactoferrin (equivalent to 49 nmole) is mixed with 100 µ.l of immobilized single-stranded DNA in 20 mM HEPES, pH 7.0 at room temperature for 10 min. The gel is washed with 500 µl of HEPES buffer five times and then suspended in equal volume of water. The amount of lactoferrin bound per bead is estimated to be 62 fmole by determining the radioactivity and counting the number of beads per unit volume. Various numbers of beads (from 1 to 12) are deposited on 0.5 mm

diameter probe tips, mixed with 0.2 µl of sinapinic acid (dissolved in 30% methanol, 0.1% trifluoroacetic acid) and analyzed by laser desorption time-of-flight mass spectrometry. Figure [[16]] 14 shows the mass spectrum of lactoferrin affinity adsorbed on a single bead of single-stranded DNA agarose. This is a representative spectrum from a total of five (average of 100 laser shots per spectrum) obtained from the single bead.

Please replace the paragraph on page 66, beginning with "2. An aliquot of 1 ml of preterm infant urine" with the following amended paragraph:

2. An aliquot of 1 ml of preterm infant urine containing 30 pmole of ^{59}Fe-human lactoferrin is mixed with 20 µl of single-stranded DNA agarose in 0.1 M HEPES pH 7.4 at 23°C for 15 min. The gel is washed with 500 µl of HEPES buffer two times and 500 µl of water two times. The gel is suspended in equal volume of water and 1 µl of the suspension (containing not more than 350 fmole of adsorbed lactoferrin as determined by radioactivity) is mixed with 1 µl of sinapinic acid (dissolved in 30% methanol, 0.1% trifluoroacetic acid) on a probe tip and analyzed by laser desorption time-of-flight mass spectrometry. Figure [[17]] 15 shows the mass spectrum of lactoferrin extracted from urine by surface immobilized DNA as the affinity capture device.

Please replace the paragraph bridging pages 66 and 67, beginning with "1. Soybean trypsin inhibitor (Sigma) is immobilized" with the following amended paragraph:

1. Soybean trypsin inhibitor (Sigma) is immobilized on AffiGel 10 (BioRad) according to manufacturer's instructions. An aliquot of 100 µl of human duodenal aspirate is mixed with 50 µl of surface immobilized soybean trypsin inhibitor at pH 7.0 (20 mM sodium phosphate, 0.5M sodium chloride) at 23°C for 15 min. The gel is then washed with 500 µl of phosphate buffer three times and 500 µl of water two times. Aliquots of 1 µl of gel suspension or the original duodenal aspirate are mixed with 2 µl of sinapinic acid (dissolved in 50% acetonitrile, 0.1% trifluoroacetic acid) and analyzed by laser desorption time-of-flight mass spectrometry.

Figure [[18A]] 16A shows the composite mass spectra of the total duodenal aspirate (lower profile) and the proteins adsorbed by surface immobilized soybean trypsin inhibitor (upper profile). The major peak in the affinity captured sample represents trypsin. Similar results are obtained with only 1 µl of duodenal fluid deposited on a) the tip of a nylon probe element coupled to soybean trypsin inhibitor via glutaraldehyde and b) the tip of an acrylic probe element coated with polyacrylamide coupled to soybean trypsin inhibitor via either glutaraldehyde or divinyl sulfone (Figure [[18B]] 16B).

Please replace the paragraph bridging pages 67 and 68, beginning with "2. Streptavidin immobilized on Dynabead" with the following amended paragraph:

2. Streptavidin immobilized on Dynabead (uniform, 2.8 µm, superparamagnetic, polystyrene beads) is obtained Dynal, AS, Oslo, Norway. Aliquots of 150 µl of human plasma or urine containing 18 pmole of biotinylated insulin (Sigma) are mixed with 20 µl suspension of streptavidin Dynabead at pH 7.0 (20 mM sodium phosphate, 0.5M sodium chloride) at 23°C for 10 min. The beads are then washed with 500 µl buffer containing 3M urea three times and 500 µl water once. Aliquots of 0.5 µl of the bead suspension are mixed with 2 µl of sinapinic acid (dissolved in 30% methanol, 0.1% trifluoroacetic acid) and analyzed by laser desorption time-of-flight mass spectrometry. Figure [[19A]] 17A shows the mass spectrum of biotinylated insulin affinity adsorbed from urine. The multiple peaks represent insulin derivatized with one to three biotin groups. Figure [[19B]] 17B shows the mass spectrum of biotinylated insulin affinity adsorbed from plasma.

Please replace the paragraph bridging pages 69 and 70, beginning with "Cibacron Blue 3GA-agarose (Type 3000," with the following amended paragraph:

Cibacron Blue 3GA-agarose (Type 3000, 4% beaded agarose, ligand density 2-5 pmoles/ml gel) is obtained from Sigma. An aliquot of 200 µl of human plasma is mixed with 50 µl of surface

immobilized Cibacron Blue at pH 7.0 (20 mM sodium phosphate, 0.5M sodum chloride) at 23°C for 10 min. The gel is then washed with 500 µl of buffer three times and 500 µl of water two times. An aliquot of 1 µl of gel suspension is mixed with 2 µl of sinapinic acid (dissolved in 50% acetonitrile, 0.1% trifluoroacetic acid) and analyzed by laser desorption time-of-flight mass spectrometry. Figure [[20]] 18 shows the selective adsorption of human serum albumin (doubly charged ion $[M+2H]^{2+}$, 32,000 m/z, singly charged ion $[M+H]^{+}$, 64,000 m/z, dimer ion, $2[M+H]^{+}$, 128,000 m/z) from the serum sample by surface immobilized Cibacron Blue (lower profile). Other immobilized dyes tested included Reactive Red 120-agarose, Reactive Blue-agarose, Reactive Green-agarose, Reactive Yellow-agarose (all from Sigma) and each selects different proteins from human plasma.

Please replace the paragraph on page 71, beginning with "1. Cinnamamide (Aldrich) (not a matrix at laser" with the following amended paragraph:

1. Cinnamamide (Aldrich) (not a matrix at laser wavelength of 355 nm by prior art) is dissolved in isopropanol: 0.5M sodium carbonate (3:1) and mixed with divinyl sulfone (Fluka, Ronkonkoma, N.Y.) activated Sepharose (Pharmacia) at 23°C for 2 hr. The excess energy absorbing molecules are washed away with isopropanol. The proposed molecular structure is presented in Figure [[21]] 19. Aliquots of 2 µl of the bound or free molecules are deposited on the probe tips, 1 µl of human estrogen receptor dimerization domain in 0.1% trifluoroacetic acid is added on top and analyzed by laser desorption time-of-flight mass spectrometry. The result shows that peptide ion signals are detected only on the bound energy absorbing molecule surface (Figure 20, top profile), the free molecules are not effective (Figure 20, bottom profile).

Please replace the paragraph on page 71, beginning with "2. Cinnamyl bromide (Aldich) (not a matrix at laser" with the following amended paragraph:

2. Cinnamyl bromide (Aldrich) (not a matrix at laser wavelength of 355 nm by prior art) is dissolved in isopropanol:0.5M sodium carbonate (3:1) and mixed with divinyl sulfone (Fluka) activated Sepharose at 23°C for 15 hr. The excess energy absorbing molecules are washed away with isopropanol. The proposed molecular structure is presented in Figure [[23]] 21. Aliquots of 2 μl of the bound or free molecules are deposited on the probe tips, 1 μl of peptide mixtures in 0.1% trifluoroacetic acid is added on top and analyzed by laser desorption time-of-flight mass spectrometry. The result shows that peptide ion signals are detected only on the bound energy absorbing molecule surface (Figure [[24]] 22, top profile), the free molecules are not effective (Figure [[24]] 22 bottom profile).

Please replace the paragraph on page 72, beginning with "3. Dihydroxybenzoic acid is activated by" with the following amended paragraph:

3. Dihydroxybenzoic acid is activated by dicyclohexylcarbodiimide and mixed with Fmoc-MAP 8 branch resin (Applied Biosystems, Forster City, Calif.) at 23°C for 15 hr. The excess energy absorbing molecules are washed away by methanol. The proposed molecular structure is presented in Figure [[25]] 23. Aliquots of 1 μl of the MAP 8 branch surface with and without bound energy absorbing molecules are deposited on the probe tips, 1 μl of peptide mixtures in 0.1% trifluoroacetic acid was added on top and analyzed by laser desorption time-of-flight mass spectrometry. The result shows that peptide ion signals are detected only on the surface with bound energy absorbing molecules (Figure [[26]] 24, bottom profile), the control surface without any energy absorbing molecules is not effective (Figure 24, top profile).

Please replace the paragraph on page 72, beginning with "4. α-cyano-4-hydorxycinnamic acid is dissolved" with the following amended paragraph:

4. α -cyano-4-[[hydorxycinnamic]]hydroxycinnamic acid is dissolved in methanol and mixed with AffiGel 10 or AffiGel 15 (BioRad) at various pHs at 23°C for 2-24 hours. The excess

energy absorbing molecules are washed away by methanol. Aliquots of 2 μl of the bound molecules are deposited on the probe tips, 1 μl of peptide mixtures or myoglobin, or trypsin or carbonic anhydrase is added on top and analyzed by laser desorption time-of-flight mass spectrometry. The result shows that myoglobin ion signal is detected on the surface with bound energy absorbing molecules (Figure [[27A]] 25) with very little contaminating low mass ion signals (Figure [[27B]] 25).

Please replace the paragraph bridging pages 72 and 73, beginning with "5. A 40% polyacrylamide solution is prepared and cast" with the following amended paragraph:

5. A 40% polyacrylamide solution is prepared and cast into the desired shape of a probe tip. The gel is allowed to air dry until no noticeable reduction in size is observed. The tip is submerged into a 9% glutaraldehyde/buffer (v/v) solution and incubated with gentle shaking at 37°C for 2 hours. After incubation, buffer is used to rinse off excess glutaraldehyde. The activated tip is added to a saturated buffered energy absorbing molecule solution and incubated at 37°C (approx.) for 24 hours (approx.) with gentle shaking. Organic solvents are used to solubilize the energy absorbing molecules in situations that required it. The tip is rinsed with buffer and placed into a 9% ethanolamine/water (v/v) solution to incubate at 25°C with gentle shaking for 30 minutes. Next, the tip is rinsed with buffer and added to a 5 mg/mL solution of sodium cyanoborohydride/buffer to incubate at 25°C for 30 minutes. Finally, the tip is rinsed well with buffer and stored until use. The same reaction is carried out on nylon tips which is prepared by hydrolysis with 6N HCl under sonication for 2 minutes and then rinsed well with water and buffer. The same reaction is also performed on acrylic tips activated by soaking in 20% NaOH for 7 days with sonication each day for 30-60 min and then washed. The proposed general molecular structure of the surface is shown in Figure [[28]] 26.

Please replace the paragraph bridging pages 73 and 74, beginning with "6. A 40% polyacrylamide solution is prepared and cast" with the following amended paragraph:

6. A 40% polyacrylamide solution is prepared and cast into the desired shape of a probe tip. The gel is air dried until no noticeable reduction in size is observed. A 0.5M sodium carbonate buffer with a pH of 8.8 is prepared as rinsing buffer. The tip is next placed into a solution of divinyl sulfone (Fluka) and buffer at a ratio of 10:1, respectively, and incubated for 24 hours. The tip is rinsed with buffer and placed into an energy absorbing molecule buffered solution at a pH of 8 to incubate for 2 hours. The same reaction is carried out on nylon tips which is prepared by hydrolysis with 6N HCl under sonication for 2 minutes and then rinsed well with water and buffer. The same reaction is also performed on acrylic tips activated by soaking in 20% NaOH for 7 days with sonication each day for 30-60 min and then washed. The proposed general molecular structure of the surface is shown in Figure [[29]] 27.

Please replace the paragraph on page 74, beginning with "7. A 40% polyacrylamide solution is prepared and cast" with the following amended paragraph:

7. A 40% polyacrylamide solution is prepared and cast into the desired shape of a probe tip. The gel is air dried until no noticeable reduction in size is observed. An energy absorbing molecule solution at 100 mg/mL in dichloromethane/NMP (2:1, respectively) and a 1M dicyclohexylcarbodiimide/NMP solution are mixed at a ratio of 1:2 (EAM:DCC), respectively. The EAM/DCC solution is next incubated at 25°C for 1 hour while stirring. After incubation, a white precipitate is observed. The white precipitate is filtered in a sintered glass filter. The flow through is the DCC activated EAM. Next, the tip is placed into the DCC activated EAM solution and incubated at 25°C for 2 hours (approx.). The tip is finally rinsed with a variety of solvents such as acetone, dichloromethane, methanol, NMP, and hexane. The same reaction is carried out on nylon tips which is prepared by hydrolysis with 6N HCl under sonication for 2 minutes and then rinsed well with water and buffer. The same reaction is also performed on acrylic tips activated by soaking in 20% NaOH for 7 days with sonication each day for 30-60 min and then washed. The proposed general molecular structure of the surface is shown in Figure [[30]] 28.

Please replace the paragraph bridging pages 75 and 76, beginning with "8. A 40% polyacrylamide solution is prepared and cast" with the following amended paragraph:

8. A 40% polyacrylamide solution is prepared and cast into the desired shape of a probe tip. The gel is air dried until no noticeable reduction in size was observed. A 100 mg/mL solution of N-α-Fmoc-N-ε-Fmoc-L-lysine in dichloromethane/NMP (2:1 respectively) and a 1M DCC/NMP solution are mixed at a ratio of 1:2 (lysine:DCC), respectively. The lysine/DCC solution is incubated at 25°C for 1 hour while stirring. After incubation, a white precipitate is observed and filtered with a sintered glass filter. The flow through is DCC activated lysine. The tip is placed into the DCC activated lysine solution and incubated at 25°C for 2 hours (approx.). The tip is next placed into 5 mL of piperidine and incubated at 25°C for 45 minutes with gentle stirring. DCC activated lysine is repeatedly reacted in consecutive cycles with the tip until the desired lysine branching is attained. An EAM solution at 100 mg/mL in dichloromethane/NMP (2:1, respectively) and a 1M DCC/NMP solution are mixed at a ratio of 1:2 (EAM:DCC), respectively. The EAM/DCC solution is incubated at 25°C for 1 hour while stirring. After incubation, a white precipitate is observed and filtered with a sintered glass filter. The flow through is the DCC activated EAM. The EAM contains an acid functional group that reacts with the DCC. The tip is placed into the DCC activated EAM solution and incubated at 25°C for 2 hours (approx.) with gentle shaking. Finally, the tip is rinsed with excess dichloromethane, NMP, and methanol before use. The same reaction is carried out on nylon tips which is prepared by hydrolysis with 6N HCl under sonication for 2 minutes and then rinsed well with water and buffer. The same reaction is also performed on acrylic tips activated by soaking in 20% NaOH for 7 days with sonication each day for 30-60 min and then washed. The proposed general molecular structure of the surface is shown in Figure [[31]] 29.

Please replace the paragraph on page 76, beginning with "1. Thiosalicylic acid (Aldrich" is dissolved in either" with the following amended paragraph:

1. Thiosalicylic acid (Aldrich) is dissolved in either water or 50% methanol in water or methanol. These solutions are either used as such or the pH of the solutions is adjusted to 6.5 with 0.5M sodium bicarbonate or ammonium hydroxide or triethylamine. Cu(II) ion are chelated by either iminodiacetate (IDA) (Chelating Sepharose Fast Flow, Pharmacia) or tris(carboxymethyl)ethyleneidamine (TED) (synthesized as described by Yip and Hutchens, 1991) immobilized on gel surface. The solutions of energy absorbing molecule are mixed with the IDA-Cu(II) or TED-Cu(II) gel at 4°C for 5 min to 15 hours. The excess energy absorbing molecules are washed away with either water or 50% methanol in water or methanol. The proposed molecular structure of the surface is shown in Figure [[32]] 30. Aliquots of 1 µl of the bound energy absorbing molecules are deposited on the probe tips, 1 µl of peptide mixtures or estrogen receptor dimerization domain or myoglobin in 0.1% trifluoroacetic acid is added on top and analyzed by laser desorption time-of-flight mass spectrometry. Figure [[33]] 31 shows one representative mass spectrum of estrogen receptor dimerization domain desorbed from this surface.

Please replace the paragraph on page 78, beginning with "Sinnapinic acid or α-cyano-4-hydroxycinnamic" with the following amended paragraph:

Sinnapinic acid or α -cyano-4-hydroxycinnamic acid are suspended in water and the pH is adjusted to 6.6 with dilute sodium hydroxide. Tentacle DEAE Fractogel (EM Separations, Gibbstown, N.J.) is washed with 20 mM HEPES, pH 6.0 and suction dried. The energy absorbing molecules solution is mixed with the DEAE gel at 23°C for 15 hours. The gel is washed with water until all excess energy absorbing molecules were removed. The proposed molecular structure of the surface is shown in Figure [[34]] 32. An aliquot of 0.5 µl of the bound energy absorbing molecules is deposited on the probe tips, 1 µl of estrogen receptor dimerization domain or myoglobin in 0.1% trifluoroacetic acid is added on top and analyzed by laser desorption time-of-flight mass spectrometry. Figures [[35]] 33A and B show the mass spectra.

Please replace the paragraph on page 78, beginning with "1. α-cyano-4-hydroxycinnamic acid is dissolved" with the following amended paragraph:

1. α-cyano-4-hydroxcinnamic acid is dissolved in 50% methanol in water and dimethylsulfoxide. This is mixed with aminomethylated polystyrene at 23°C for 15 hours. The excess energy absorbing molecules are washed away with 50% methanol in water. The proposed molecular structure is shown in Figure [[36]] 34. An aliquot of 1 µl of the bound energy absorbing molecules is deposited on the probe tip, 1 µl of peptide is added on top and analyzed by laser desorption time-of-flight mass spectrometry.